REMARKS

The Office Action dated July 8, 2005 has been carefully reviewed, and the following remarks are made in response thereto. In view of the above following remarks, Applicants respectfully request reconsideration and reexamination of this application and timely allowance of the pending claims.

Applicants would like to thank the Examiner for withdrawing the species election.

Status of Claims

Upon entry of the instant amendment, claims 2-7, 11, 13, 13, 16, 19, 31, 38, and 46-60 will be pending.

Amendments of the Claims

Claims 2, 4, 7, 19, 31, 38, 51 and 56 have been amended. The amendments to the claims do not add prohibited new matter. Support for the amendments are summarized below.

Support for the amendment of claim 2 and 38 can be found in original claim 37 and on page 8, line 5, which discloses that the formulation need not include a liposome and the formulation is applied to the skin of a subject, respectively. Applicants point out that the claims as filed in the original specification are part of the disclosure (see MPEP 2163.06(III) and 35 U.S.C. § 112, Second Paragraph). Therefore, original claim 37 provides support for the amendments to claims 2 and 38.

Support for the amendment of claim 7 can be found on page 22, line 23 which discloses genetically detoxified toxins.

Support for the amendment of claim 19 and 56 can be found on page 19, line 31 to line 32 which discloses that a single molecule can be an adjuvant and an antigen.

Information Disclosure Statement

According to the Office Action, the foreign documents and non-patent literature listed on information disclosure statement (IDS) submitted on February 23, 2004 were not considered because the references were not available.

Applicants respectfully point out that according to MPEP 609 (I)(A)(2), documents submitted in a prior application need not be resubmitted in the present application under examination if the present application claims the benefit of the prior application under 35 U.S.C. § 120.

Applicants would like to thank the Examiner for her phone call informing Applicants' agent that the references in the parent application have been found and that Applicants need not supply another copy of the references for the Examiner's consideration. Applicants look forward to receiving the initialed copy of Form PTO 1449 after the Examiner considers the listed references.

Claim Rejections under 35 U.S.C. § 112, First Paragraph

A. Claims 2-7, 11, 13-14, 16, 19 and 31 have been rejected under 35 U.S.C. § 112, first paragraph, because the specification does not contain sufficient written description for the claimed invention.

The Office Action alleges that the specification as filed does not provide written description or set forth the metes and bounds of the phrases "the formulation is applied in the amount and for a length of time effective to induce an immune response specific for the at least one antigen" and "genetically altered toxin."

Without acquiescing to the propriety of this rejection, Applicants have amended claim 2 to remove the language objected to for the sole purpose of advancing prosecution. In addition, Applicants have removed "genetically altered toxin" from claim 7 and replaced it with "genetically detoxified toxin." Support for this amendment can be found throughout the specification, specifically on page 22, line 23. In view of the claim amendments, Applicants respectfully request that this rejection be withdrawn.

B. Claims 2-7, 11, 13-14, 16, 19, 31, 38 and 46-60 have been rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the enablement requirement.

The Office Action asserts that the specification does not reasonably provide enablement for a method of inducing an immune response by applying a formulation to intact skin of subject wherein the formulation is comprised of at least one antigen and at least one adjuvant wherein the formulation is applied in dry form. The Office Action also alleges that the Examples in the specification either pretreat with aqueous media or apply an adjuvant formulation in aqueous form and that there is no immune response without pretreatment of the skin.

Respectfully, Applicants point out the claims, as they stand, are directed to a method of inducing an immune response comprising applying a formulation to skin of a subject, wherein the formulation comprises at least one antigen and at least one adjuvant, wherein the formulation is applied in dry form, and wherein the formulation does not include a liposome. Additionally, it is pointed out that the specification clearly demonstrates in Example 1 that a dry powder formulation of Cholera toxin (CT) induced high levels of antibodies in mice when applied to skin (see, *e.g.*, page 38, lines 3 to 8). The data in Table 1 confirm that mice immunized on the skin with CT achieved high titers of antibody without pretreatment (see Table 1, mice numbers 996, 997, 998, 999). Additionally, the data in Tables 2 and 3 summarize similar results for Examples 2 and 3, respectively, using immunizations with reduced amounts of CT (50 μg and 25 μg respectively) in powder form applied to the skin.

In addition, Examples 4 through 7 disclose data that show that dry formulations of different antigens induce an immune response when placed on the skin. In each Example, a specified amount of an antigen solubilized in a liquid solution was allowed to dry overnight to achieve a dry formulation. Then the dry formulation was placed on the skin of mice to test for an induction of an immune response. The data collected show an immune response to each antigen when a dry formulation of each antigen was placed on the skin of mice.

Thus, these data clearly demonstrate that a dry powder formulation applied directly to the skin without pretreatment does induce an immune response. The Examples describe in detail how the immunizations were accomplished thus teaching one skilled in the art how to use the claimed invention.

Therefore, in stark contrast to the statements made in the Office Action, the specification does provide sufficient guidance to enable one of ordinary skill in the art to make and use a dry formulation of antigens for inducing an immune response without undue experimentation. Applicants respectfully point out that the Examples in the specification describe in detail how the dry formulations are made, how they are applied, and how to test for induction of an immune response. Therefore, the specification satisfies the requirements of enablement set forth by the Wands factors. Applicants respectfully request that this rejection be withdrawn.

Claim Rejections under 35 U.S.C. § 102

A. Claims 2-5, 7, 11, 13, 14, 16, 19, 31, 38, 46-48, 51-54, 56, 58-60 have been rejected under 35 U.S.C. § 102 (e) as being anticipated by U.S. Patent 5,910,306.

The Office Action alleges that the patent teaches that a liposome containing an antigen and adjuvant can be lyophilized and applied to the skin of said subject. Applicants have amended independent claims 2 and 38 to recite "wherein the formulation does not include a liposome." Support for this amendment can be found at least in original claim number 37. As discussed above, the claims as filed in the original specification are part of the disclosure (see MPEP 2163.06(III) and 35 U.S.C. § 112, Second Paragraph). Claims 3-5, 7, 11, 13, 14, 16, 19, 31, 46-48, 51-54, 56, and 58-60 all depend on either claim 2 or 38, thus incorporating all of their limitations. Thus, in view of the claim amendments to claims 2 and 38, U.S. Patent 5,910,306 does not anticipate these claims. Therefore, Applicants respectfully request that this rejection be withdrawn.

B. Claims 2-7, 11, 13, 14, 16, 19, 31, 38, and 46-60 have been rejected under 35 U.S.C. § 102 (e) as being anticipated by U.S. Patent 5,980,898.

The Office Action alleges that the patent teaches that a liposome containing an antigen and adjuvant can be lyophilized and applied to the skin of said subject. As discussed immediately above, Applicants have amended claims 2 and 38 to recite "wherein the formulation does not include a liposome." Claims 7, 11, 13, 14, 16, 19, 31, and 46-60 depend on either claim

2 or 38, thus incorporating all of their limitations. Thus, in view of the claim amendments to claims 2 and 38, U.S. Patent 5,980,898 does not anticipate these claims. Therefore, Applicants respectfully request that this rejection be withdrawn.

Claim Rejections under 35 U.S.C. § 103

Claims 2, 6, 49, 55 and 57 have been rejected under 35 U.S.C. § 103 (a) as being unpatentable over U.S. Patent 5,910,306 and U.S. Patent 5,988,898.

Applicants have amended claims 2 and 38 to recite "wherein the formulation does not include a liposome." Claims 6, 49, 55 and 57 are dependent upon claims 2 or 38, thus incorporating all of their limitations. The claims as they stand are directed to a method of inducing an immune response comprising applying a formulation in dry form to a subject, wherein the formulation does not include liposomes. Accordingly, the cited patents to not render the claims obvious. Thus, Applicants respectfully request that this rejection be withdrawn.

Non-Statutory Double Patenting

The claims have been provisionally rejected under the judicially created doctrine of double patenting. Specifically, the claims have been rejected over claim 1 of copending Application 11/109,948 and claim 1 of Application 10/435,676.

Respectfully, Applicants would like to point out that the claims of the present invention are directed to a method of inducing an immune response comprising applying a dry formulation to skin of a subject. Although the claims of Application 11/109,948 are directed to a method of inducing an immune response, these claims do not comprise applying a formulation in dry form to the skin of a subject. Likewise, unlike the claims of the present application, the claims of Application 10/435,676 are directed to transcutaneous immunostimulation by applying an adjuvant epicutaneously to the skin and immunizing the subject by another route. Therefore, Applicants assert that the claims in the instant application are patently distinct from the pending applications. Thus, Applicants request that this rejection be withdrawn.

CONCLUSION

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration, and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, they are invited to telephone the undersigned at their convenience.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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